Electrospray Mass Analysis of Chemical Oxidation of 1,2-Diarylcyclopropanes by Cu(II) Salt

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Electrospray ionization mass spectrometry was used to study chemical electron-transfer reactions of 1,2-diarylcyclopropanes by Cu(II) salt in acetonitrile. The ion $[M - H]^+$ with a hydrogen atom loss and the solvent adduct ions, $[M+42]^+$, etc., were detected as the initial reaction products, where $[M+42]^+$ represents the ion whose mass is 42 u greater than the parent molecule M. From the study of deuterated derivatives, the hydrogen abstraction was revealed to occur at the 3 position of the cyclopropanes, and the mechanism of the hydrogen abstraction reaction and of the solvent addition were discussed. (J Am Soc Mass Spectrom 1998, 9, 966–969) © 1998 American Society for Mass Spectrometry

In recent years, there has been much interest on the synthesis and mechanism of the formation of reactive species in electron transfer reaction involving a small ring compound. For example, one electron oxidation of 1,2-diarylcyclopropane was observed by photochemical [1, 2] and electrochemical reaction [3] via *cis–trans* isomerization as described below:

$$cis\text{-CP} \xrightarrow{h\nu} cis\text{-CP}^{\bullet +}$$

$$cis\text{-CP}^{\bullet +} \rightarrow \text{CP(open)}^{\bullet +}$$

$$\text{CP(open)}^{\bullet +} \rightarrow trans\text{-CP}^{\bullet +}$$

$$trans\text{-CP}^{\bullet +} + cis\text{-CP} \rightarrow trans\text{-CP} + cis\text{-CP}^{\bullet +}$$

The formation of both *cis*-cyclopropane (*cis*-CP) and *trans*-cyclopropane by γ-irradiation of 1,2-diarylcyclopropane was also detected by absorption spectroscopic analysis [2]. However, the expected important reaction intermediate, 1,3-diarylpropene radical cation as expressed by CP(open)$^{\bullet +}$ in the scheme, has neither been trapped nor detected.

More recently, electrospray ionization mass spectrometry (ESI-MS) has been used as a powerful technique to determine the molecular weight of nonvolatile or thermally unstable compounds [4–6]. ESI-MS is a very soft ionization process that can extract ionic species directly from solution into gas phase without any ion fragmentation. In addition, the high sensitivity of ESI-MS detection provides an effective means of detecting reaction intermediates. This characteristic feature of ESI-MS has been utilized by Sam et al. [7] to identify the active BML (bleomycin) intermediate as HOO–Fe(III)BML in the reaction of BML and H_2O_2. Que et al. [8] reported the use of ESI-MS to identify the unstable species produced by the reaction between a nonheme iron complex and dioxygen or peroxide in a low temperature mixer. Arakawa et al. [9] also reported the detection and characterization of the initial ionic products during the photoinductive electron transfer reaction of dicyanobenzene and allylic silane by ESI-MS. Van Berkel et al. [10–13] have demonstrated that use of chemical electron-transfer reactions in ESI-MS was an effective method to ionize neutral organic compounds in solution. Highly conjugated molecules, metalloporphyrins, and aromatic compounds were detected as radical cations or dications in chemical oxidation with electron-transfer reagents of 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) and antimony pentafluoride (SbF_5). Xu et al. [14] have also demonstrated that some easily oxidized compounds such as metallocenes and polycyclic aromatic hydrocarbons can be ionized at the ESI needle by electrochemical oxidation processes and be detected as radical cations in the ESI mass spectra.

We report here chemical oxidation of 1,2-diarylcyclopropane by Cu(II) salt, and attempt to identify the

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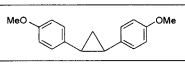
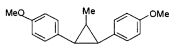
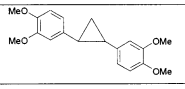
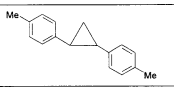
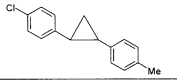
Table 1. Structural formula and detected peaks in ESI mass spectra

compounds	structural formula	detected peaks[a]
1,2-bis(4-methoxyphenyl)-cyclopropane, 1		$[M-H]^+$ $[M+42]^+$, $[M+58]^+$, $[M+74]^+$
1,1,2,2-tetraphenylcyclo-propane, 2		$[M-H]^+$ $[M+15]^+$, $[M+77]^+$, $[M+118]^+$
1,2-bis(4-methoxyphenyl)-3-methylcyclopropane, 3		$[M-H]^+$ $[M+42]^+$, $[M+58]^+$, $[M+74]^+$ $[M+99]^+$, $[M+145]^+$
1,2-bis(3,4-dimethoxyphenyl)-cyclopropane, 4		$[M-H]^+$ $[M+58]^+$
1,2-bis(*p*-tolyl)-cyclopropane, 5		$[M-H]^+$ $[M+15]^+$, $[M+42]^+$, $[M+58]^+$, $[M+74]^+$
1-(*p*-chlorophenyl)-2-(*p*-tolyl)-cyclopropane, 6		$[M+58]^+$, $[M+74]^+$
1,2-diphenylcyclopropane, 7		$[M-H]^+$ $[M+15]^+$, $[M+74]^+$
1,1,2-triphenyl-1-methylcyclo propane, 8		$[M-H]^+$ $[M+15]^+$, $[M+58]^+$, $[M+74]^+$

[a] $[M-H]^+$ represents an ion with hydrogen atom loss, and $[M+42]^+$ does an ion that has mass 42 amu greater than a molecule, M.

intermediate radical cation $CP(open)^{\bullet+}$ and its respective products using ESI-MS.

Experimental

A sector type mass spectrometer (JEOL-D300) connected to a laboratory-made ESI interface was used for ESI-MS experiments. All cyclopropane samples were dissolved in high purity acetonitrile and degassed for several minutes by nitrogen before measurement. $Cu(BF_4)_2$ was added to the samples and the ESI mass spectrum was obtained. The concentration of cyclopropane derivatives and $Cu(BF_4)_2$ was both at 1 mM, and the time elapsed from the addition of Cu(II) salt to the determination of the mass spectrum was about 1 min.

Results and Discussion

The positive ion ESI mass spectrum of 1,2-bis(4-methoxyphenyl)-cyclopropane **1** (Table 1) with Cu(II) in acetonitrile solution was shown in Figure 1. The spectrum shows two ions m/z 104 and 145, corresponding to the monovalent copper ions solvated with acetonitrile (AN), $Cu(AN)^+$, and $Cu(AN)_2^+$. In addition, the spectrum shows four reaction product ions of 1,2-bis(4-methoxyphenyl)-cyclopropane (molecular weight M) at $[M-H]^+$, $[M+42]^+$, $[M+58]^+$, and $[M+74]^+$. When $Cu(BF_4)_2$ was added to the colorless sample, the solution immediately turned reddish violet and changed to light blue color after 10 min. When the sample, changed to the light blue color, was electrosprayed, no signal other than the solvated copper ions was detected. The previous work [2] has suggested that the change to the reddish violet solution could be accounted for by the

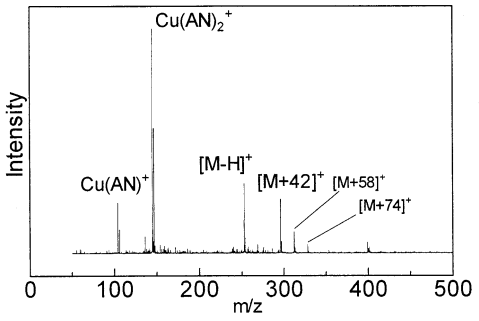


Figure 1. Positive ion ESI mass spectra for 1,2-bis(4-methoxyphenyl)-cyclopropane **1** (1 mM)+$Cu(BF_4)_2$ (1 mM) in acetonitrile.

formation of cationic species, which has not been detected by the absorption spectroscopy. In this study we can identify $[M-H]^+$ or the solvent adduct ions as an origin of the reddish violet. Our ESI spectrum did not contain a peak that can be assigned to the radical cation such as $CP(open)^{\bullet+}$. Instead of $Cu(BF_4)_2$, nonoxidizing reagent $NaBF_4$ was added with the same concentration as $Cu(BF_4)_2$ to make electrolytic effects clear. Although the $NaBF_4$ solution was colorless, $[M-H]^+$ was observed with much less intensity than that of the $Cu(BF_4)_2$ solution. This formation of $[M-H]^+$ is because of the electrochemical oxidation process [14] at the ESI needle.

In order to identify the position of the hydrogen atom loss in the formation of electron transfer reaction product $[M-H]^+$, the ESI spectrum of 1,1,2,2-tetraphenylcyclopropane **2**, was obtained under the same condition as shown in Figure 2. The spectrum detected the same type of ions, $Cu(AN)^+$, $Cu(AN)_2^+$, and $[M-H]^+$, and indicates that the hydrogen abstraction did not occur at the 1 or 2 position but might be at the 3 position. In additions, other peaks of $[M+15]^+$, $[M+77]^+$, and $[M+118]^+$ were observed in the spectrum. The compound with deuterium substitution at the 3 position, 1,1,2,2-tetraphenyl-3,3-dideuteriocyclopropane was then studied to make sure of the origin of the hydrogen atom. The ESI spectrum was obtained on-line using a low temperature mixer as shown in Figure 3. The low temperature mixer was used in an effort to

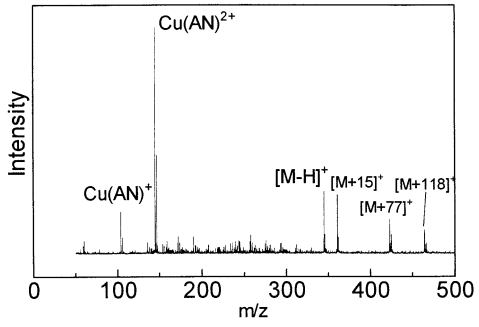


Figure 2. ESI mass spectra for 1,1,2,2-tetraphenylcyclopropane **2**+$Cu(BF_4)_2$ in acetonitrile.

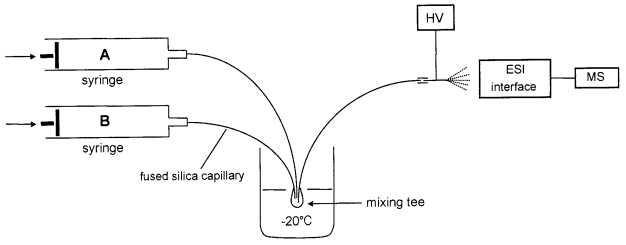


Figure 3. Low-temperature mixing apparatus. Solution A: cyclopropane derivative in acetonitrile, B: $Cu(BF_4)_2$ in acetonitrile.

increase the reaction of $[M - D]^+$ production, to suppress side reactions, and to promote the $[M - D]^+$ ion detection. The resulting ESI spectrum is shown in Figure 4. The deuterated compound was a mixture of di-, mono-, and none-deuterated. Therefore, the calculated isotope distribution of the mixture in the insert of Figure 4 was obtained by the following procedures. First, the composition ratio of the mixture was determined to be 100:96:13 by gas chromatography-mass spectrometry analysis. The isotope distribution for the mixture at near m/z 346 of Figure 4 was calculated assuming that abstraction of the hydrogen atom and the deuterium atom occurs with the same probability. The calculated distribution is nearly identical with that obtained in the ESI spectrum. The detection of the $[M - D]^+$ ions in the 3-substituted deuterated derivative clearly indicates that the hydrogen abstraction has occurred at position 3.

Van Barkel et al. [10, 11] have reported that in the ESI mass spectra of highly conjugated molecule, β-carotene, $[M - H]^+$ and dication M^{2+} were detected via the chemical oxidation, and suggested that $[M - H]^+$ resulted from proton loss of the dication, as expressed by $[M^{2+} - H^+]^+$. Dications are much more reactive than monocations. The redox potentials for $Cu(II) + e^- \rightarrow Cu(I)$ is $E^0 = 0.153$ V vs. SCE. The oxidation

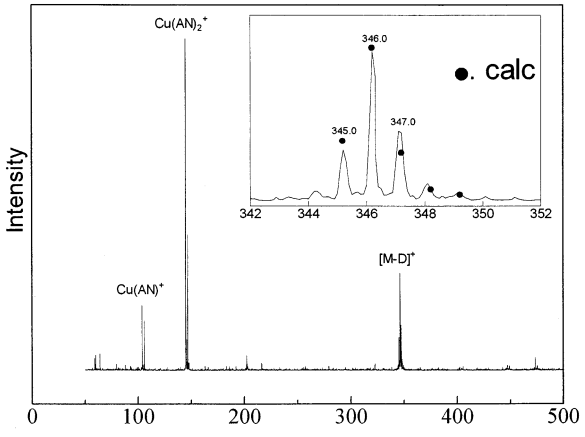
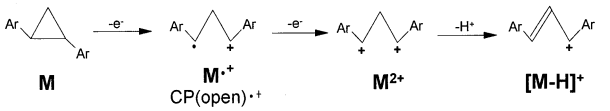


Figure 4. ESI mass spectrum for 1,1,2,2-tetraphenyl-3,3-dideuteiocyclopropane+$Cu(BF_4)_2$ in acetonitrile, measured by low-temperature mixing apparatus (Figure 3). The closed circle in the inset shows the calculated isotope distribution of the deuterated compound.



Scheme I

potential of $CP \rightarrow CP^+ + e^-$ for **1** (*cis*) is $E^0_{0x} = 0.65$ V vs. Ag/Ag^+ [1]. A two step oxidation is a probable process via distonic cation intermediate. As a result, Scheme I is proposed for the formation of $[M - H]^+$ in the chemical oxidation of 1,2-diarylcyclopropane. However, the dication was not able to be detected under the present ESI conditions.

In order to characterize ions other than $[M - H]^+$, 1,2-bis(4-mehoxyphenyl)-3-methyl-cyclopropane **3**, was studied. Its ESI spectra in acetonitrile and in acetonitrile-d_3 are shown in Figure 5a, b, respectively. In Figure 5a, the $[M - H]^+$ appeared as a low intensity ion as expected from the fact that only one of the hydrogen atom remains at the 3 position. In addition, peaks of $[M+42]^+$, $[M+58]^+$, $[M+74]^+$, $[M+99]^+$, and $[M+145]^+$ are detected in the spectrum 5a and peaks of $[M+45]^+$, $[M+61]^+$, $[M+77]^+$, $[M+105]^+$, and $[M+151]^+$ are detected in the spectrum 5b. When the two spectra are compared, the $[M+42]^+$, $[M+58]^+$, and $[M+74]^+$ ions of spectrum 5a appears at 3 mass units higher in spectrum 5b and are assigned as the adduct ions of one acetonitrile molecule. Similarly, the ions $[M+99]^+$ and $[M+145]^+$ appears at 6 mass units higher in spectrum 5b. Therefore, they can be assigned to the adduct ions of two acetonitrile molecules. In an analogy to the proposed mechanism of the $[M - H]^+$ formation, Scheme II is proposed for the formation of the acetonitrile adduct

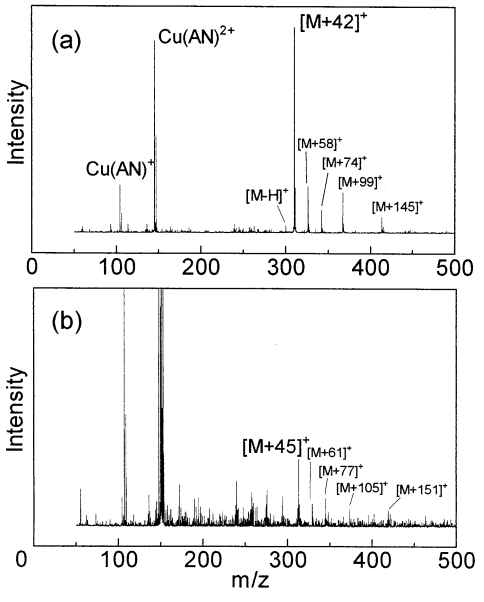
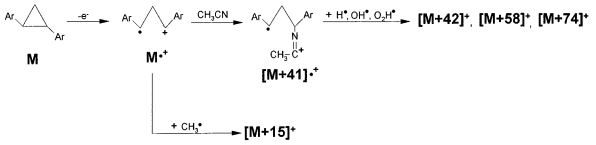


Figure 5. ESI mass spectra for 1,2-bis(4-methoxyphenyl)-3-methylcyclopropane **3**+$Cu(BF_4)_2$: (**a**) in acetonitrile and (**b**) in acetonitrile-d_3.



Scheme II

ions. The proposed reaction mechanism is in agreement with that of the Ritter reaction [15].

ESI-MS measurements were also carried out with other 1,2-diarylcyclopropane derivatives, **4–8**, listed in Table 1. As expected, $[M - H]^+$ ions were detected in all derivatives that possess hydrogen atoms in the 3 position.

Conclusions

In the present ESI-MS study, we could not detect the radical cation of the CP(open)$^{\bullet+}$ ion. Instead, we detected and identified the hydrogen atom loss ion $[M - H]^+$ and the solvent adduct ions. The origin of the reddish violet color is not CP(open)$^{\bullet+}$, but $[M - H]^+$ or the solvent adduct ions. The failure to detect a CP(open)$^{\bullet+}$ may be because of the following reasons: the lifetime of the intermediate is much shorter than a millisecond, or an electrolytic oxidation of the unstable intermediate by high voltage applied at the needle tip is taking place in the electrospray source. However, the detection of the $[M - H]^+$ ion suggests that the reaction must proceed through an CP(open)$^{\bullet+}$ intermediate as shown in Scheme I.

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